

ATENT COOPERATION TRE TY

	PCT	
--	-----	--

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

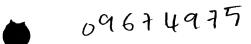
To:

Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ÉTATS-UNIS D'AMÉRIQUE

Date of mailing (day/month/year) . 09 March 2000 (09.03.00)	in its capacity as elected Office Applicant's or agent's file reference MSKP039WO	
International application No. PCT/US99/10065		
International filing date (day/month/year) 07 May 1999 (07.05.99)	Priority date (day/month/year) 08 May 1998 (08.05.98)	
Applicant		
AGUS, David, B. et al		

1.	The designated Office is hereby notified of its election made:				
	X in the demand filed with the International Preliminary Examining Authority on: 01 December 1999 (01.12.99)				
	in a notice effecting later election filed with the International Bureau on:				
2.	The election X was				
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).				

	Authorized officer
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

REC'D 23 OCT 2000
PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MSKP039WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)		
International application No.	International filing date (day/r	month/year) Priority date (day/month/year)		
PCT/US99/10065	07 MAY 1999	08 MAY 1998		
International Patent Classification (IPC) IPC(7): A01N 37/18 and US Cl.: 514	or national classification and II 4/2, 12	PC		
Applicant SLOAN-KETTERING INSTITUTE F	OR CANCER RESEARCH			
This international prelimina Examining Authority and is	ary examination report has transmitted to the applicant	been prepared by this International Preliminary according to Article 36.		
2. This REPORT consists of a	total of 4 sheets.			
This report is also accombeen amended and are the (see Rule 70.16 and Section 1).	panied by ANNEXES, i.e., she le basis for this report and/or sh tion 607 of the Administrative	neets of the description, claims and/or drawings which have neets containing rectifications made before this Authority. Instructions under the PCT).		
These annexes consist of a to	otal of sheets.			
3. This report contains indications relating to the following items: I X Basis of the report II Priority III Non-establishment of report with regard to novelty, inventive step or industrial applicability IV Lack of unity of invention V X Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI Certain documents cited				
VII Certain defects in the international application VIII Certain observations on the international application		ation		
Date of completion of the demand Date of completion of this report				
Date of submission of the demand	l Da	or combination or any columnia		
01 DECEMBER 1999		02 OCTOBER 2000		
Name and mailing address of the IPEA Commissioner of Patents and Trade Box PCT Washington, D.C. 20231	100	SURAN WAGAR SULLO OF W		
Facilità No. (703) 305-3230	Te	lephone No. (703) 308-0196		

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.	
PCT/US99/10065	

L B	asis f the re	ep rt			
1. With	regard to the	elements of the interna	ational application:*		
x		ional application as			
	the descript				
X	nages	1-12		, as originally filed	
	pages	NONE		, filed with the demand	
	pages	NONE	, filed with the letter	of	
_					
X	the claims:	12 15		, as originally filed	
	pages		as amended (togeth	ner with any statement) under Article 19	
	pages	NONE		filed with the demand	
	pages	NONE	, filed with the letter of		
X				as originally filed	
	pages			, as originally filed , filed with the demand	
	pages		filed with the letter of	of	
	pages	NONE	, med with the letter		
X	the sequence	ce listing part of the	description:		
	pages	1-13		, as originally filed	
		NONE		. filed with the demand	
	pages	NONE	, filed with the letter	of	
	the language or 55.3).	ge of the translation fur		preliminary examination (under Rules 55.2 and	
3. W	ith regard to reliminary ex	any nucleotide and/	or amino acid sequence disclosed in the dout on the basis of the sequence list	he international application, the international ting:	
X	contained	in the international	application in printed form.		
[x			itional application in computer reada	ble form.	
뜯			Authority in written form.		
늗	_1		Authority in computer readable form	m.	
	IJ □ The states	nent that the subseque	ently furnished written sequence listing d has been furnished.	g does not go beyond the disclosure in the	
	The statem been furnis	ent that the information	on recorded in computer readable form is	s identical to the writen sequence listing has	
	٦		ed in the cancellation of:		
4.			NONE		
		description, pages_			
		claims, Nos.	NONE NONE		
_	X the	drawings, sheets/fi	· B	made gines they have been considered to an	
5. X This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**					
1	beyond the	ha dissilomes as tiled (as maicaied iii die supplementat dox (ixt		
) ü				to an invitation under Article 14 are referred to they do not contain amendments (Rules 70.16	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10065

V.	Reas ned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
	citations and explanati ns supp rting such statement

1.	statement			
	Novelty (N)	Claims	3, 4, 7-11	YES
		Claims	1, 2, 5, 6	NO
	Inventive Step (IS)	Claims	3, 4, 7-11	YES
	•	Claims	1-2, 5-6	NO NO
	Industrial Applicability (IA)	Claims	I-11 ·	YES
		Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by US Patent No. 5,550,214.

The claims are drawn to a method for active vaccination against autologous cells (B cells) expressing transmembrane proteins comprising administering a vaccine composition comprising an immunogenic portion of the extracellular domain of the transmembrane protein with a carrier protein effective to break tolerance to the transmembrane protein and a pharmaceutically acceptable adjuvant wherein the transmembrane protein is Her2-neu.

US Patent No. 5,550,214 teaches a method for active peptide vaccine wherein the immunogen is HER2/neu wherein a pharmaceutically-acceptable carrier is included (col 17, lines 60-65, wherein the carrier is a protein such as BCG, wherein an adjuvant is included and is selected from a group including Freund's complete or incomplete adjuvant (col 19, lines 51-65). It would be an inherent property of the method to vaccinate against B cells.

In the Response to PCT/IPEA/408 submitted 24 April 2000, Applicant traverses the instant objection.

Applicant argues that the cited reference peptides are not drawn to an extracellular domain and states that a copy of a summary sheet is attached. The argument has been considered but has not been found persuasive because no summary sheet has been attached and therefore could not be considered and because the '214 patent specifically states that the peptide are recognized y cancer-specific CTL's for a variety of sources (col 5) and it would be expected that this reaction would be to an extracellular epitope

Claims 1-2 and 5-6 lack novelty under PCT Article 33(2) as being anticipated by US Patent No. 5,726,023.

The claims are drawn to a method for active vaccination against autologous cells (B cells) expressing transmembrane proteins (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10065

Sup	plem	ntal	В	3
-----	------	------	---	---

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

- I. BASIS OF REPORT:
- (Some) amendments are considered to go beyond the disclosure as filed: NONE
- V. 2. REASONED STATEMENTS CITATIONS AND EXPLANATIONS (Continued):

comprising administering a vaccine composition comprising an immunogenic portion of the extracellular domain of the transmembrane protein with a carrier protein effective to break tolerance to the transmembrane protein and a pharmaceuticall acceptable adjuvant wherein the transmembrane protein is Her2-neu wherein the carrier protein is KLH.

US Patent No. 5,726,023 teach a method for active vaccination against autologous cells comprising an immunogenic portion Her2-neu wherein the vaccine comprises the immunogen, Her-2/neu, and adjuvant and wherein the immunogen is coupled to KLH (col 14, lines 15-47). It would be an inherent property of the method to vaccinate against B cells.

In the Response to PCT/IPEA/408 submitted 24 April 2000, Applicant traverses the instant rejection.

Applicant argues that the '023 patent teaches the preferred use of peptides derived from amino acids 676-1255 and specifically states that the entire extracellular domain without some other portions of protein is not used. The argument has been considered but has not been found persuasive because the claims are specifically drawn to a vaccine comprising at least an immunogenic portion of the extracellular domain. The cited references clearly teaches vaccines comprising peptides not only of the cytoplasmic portion but also of the extracellular domain.

Claims 3-4, 7-11 meet the criteria set out in PCT Article 33(3)-(4), because the prior art does not teach or fairly suggest a method wherein the immunogen is SEQ ID NO:1 or 2.

claims 1-11 meet the criteria set out under PCT Article 33(4).

----- NEW CITATIONS -----

Harlow and Lane, 1988, Antibodies a Laboratory Manuarl, Cold Spring Harbor Laboratory, Cold Spring Harbor, p. 72.



INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/10065

Group III

Claim 13 is generic to a plurality of distinct species which are transmembrane proteins that are different in structure and function wherein the transmembrane proteins are:

Species A - CD20 (claims 14-20)

Species B - Her2-neu (claims 14 and 18)

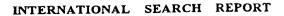
Species C - VEGF Receptor (claims 14 and 18)

Species D - epidermal growth factor receptor (claims 14 and 18)

Species E - CD19 ((claims 14 and 18)

Species F - interleukin-2-receptor (claims 14 and 18) Species G - interleukin-4-receptor (claims 14 and 18)

Species H - P-glycoprotein (claims 14 and 18)



International application No. PCT/US99/10065

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

GENESEQ, SWISS-PROT, SPTREMBL, APS, EMBASE, BIOSIS, MEDLINE, CAPLUS, DRUGU, PROMT, SCISEARCH, CANCERLIT, LIFESCI, TOXLINE, PHIN search terms: vaccin?, CD20, her2, neu, erbb2

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-11, drawn to a method for active vaccination against autologous cells expressing transmembrane

Group II, claim(s) 12 drawn to a method for treatment of B cell non-Hodgkin's lymphoma.

Group III, claim(s) 13-20, drawn to a vaccine composition.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking groups I-III appears to be that they all relate to a method for active vaccination with at least an immunogenic portion of the extracellular domain of a transmembrane protein.

However, Hooijberg et al (J. Immunother. Emphasis Tumor Immunol, 1996, 19(5), 346-356 specifically teaches a method of active immunization with at least an immunogenic portion of the extracellular domain of a transmembrane protein wherein that protein is CD19, wherein that protein is CD20 (see abstract).

Therefore, the technical feature linking the inventions of Groups I-III does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be a method for active vaccination.

The special technical feature of Group II is considered to be a method of treatment.

The special technical feature of Group III is considered to be a vaccine composition.

Accordingly Groups I-III are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I

Claim 1 is generic to a plurality of distinct species which are transmembrane proteins that are different in structure and function wherein the transmembrane proteins are:

Species A - CD20 (claims 2-11)

Species B - Her2-neu (claims 2 and 6)

Species C - VEGF Receptor (claims 2 and 6)

Species D - epidermal growth factor receptor (claims 2 and 6)

Species E - CD19 (claims 2 and 6)

Species F - interleukin-2-receptor (claims 2 and 6)

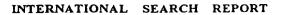
Species G - interleukin-4-receptor (claims 2 and 6)

Species H - P-glycoprotein (claims 2 and 6)

INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/10065

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:	
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
Please See Extra Sheet.	
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searc claims.	hable
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite pay of any additional fee.	ment
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report conly those claims for which fees were paid, specifically claims Nos.: 1-11	DVers
4. No required additional search fees were timely paid by the applicant. Consequently, this international search represented to the invention first mentioned in the claims; it is covered by claims Nos.:	ort is
Remark on Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees.	



International application No.
PCT/US99/10065

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) :A01N 37/18				
US CL :5 According to	o International Patent Classification (IPC) or to both	national classification and IPC		
B. FIELI	DS SEARCHED			
Minimum do	cumentation searched (classification system follower	d by classification symbols)		
U.S. :	514/2, 12			
Documentation	on searched other than minimum documentation to the	extent that such documents are included	in the fields searched	
Electronic da	ata base consulted during the international search (na	ame of data base and, where practicable,	search terms used)	
Please See	Extra Sheet.			
c. Doct	UMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.	
х	Database BIOSIS, AN 1997:22684, In Syngeneic Tumor B Cells by Autoreact Specific for a CD19 Antigen-Deriv Immunoth. 1996, Vol. 19, No. 5, page Abstract.	ive Cytotoxic T Lymphocytes ved Synthetic Peptide. J.	1-11	
x	US 5,550,214 A (EBERLEIN et al.) 27 August 1996, see especially 1,2,5,6 cols 17-22.			
X US 5,726,023 A (CHEEVER et al.) 10 March 1998, see especially 1,2,5,6 cols 3, 13, 14.				
Further documents are listed in the continuation of Box C. See patent family annex.				
Special categories of cited documents: T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand.				
	A document defining the general state of the art which is not considered the principle or theory underlying the invention to be of particular relevance			
"E" carlier document published on or after the international filing date "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step				
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other				
special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination				
means being obvious to a person skilled in the art				
P document published prior to the international filing date but later than *&* document member of the same patent family the priority date claimed				
Date of the actual completion of the international search Date of mailing of the international search report				
10 AUGUST 1999 29 SEP 1999				
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Authorized officer SUSAN UNGAR				
	Facsimile No. (703) 305-3230 Telephone No. (703) 308-0196			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
вј	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Vict Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
СН	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein .	SD	Sudan		
DK	Denmark	LK.	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		